

PS



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/706,768      | 11/12/2003  | Gerd Ascher          | G-970-9856F         | 7767             |

1095 7590 06/06/2005

NOVARTIS  
CORPORATE INTELLECTUAL PROPERTY  
ONE HEALTH PLAZA 104/3  
EAST HANOVER, NJ 07936-1080

EXAMINER

BERCH, MARK L

ART UNIT PAPER NUMBER

1624

DATE MAILED: 06/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                                      |                                      |  |
|------------------------------|--------------------------------------|--------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/706,768 | <b>Applicant(s)</b><br>ASCHER ET AL. |  |
|                              | <b>Examiner</b><br>Mark L. Berch     | <b>Art Unit</b><br>1624              |  |

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 16-27 is/are pending in the application.
- 4a) Of the above claim(s) 22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 16-21 and 23-27 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☒ Certified copies of the priority documents have been received in Application No. 09/381,758.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>1/22/04</u> . | 6) <input type="checkbox"/> Other: ____.  |

*pd*

Art Unit: 1624

## DETAILED ACTION

### *Election/Restrictions*

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claims 16-21, 23-27, drawn to Cephalosporins, synthesis and use, classified in class 540; 514, subclass 222; 202.
- II. Claim 22, drawn to piperazine intermediates, classified in class 544, subclass 398, 402.

The inventions are distinct, each from the other because of the following reasons:

Inventions I and II are related as mutually exclusive species in an intermediate-final product relationship. Distinctness is proven for claims in this relationship if the intermediate product is useful to make other than the final product (MPEP § 806.04(b), 3rd paragraph), and the species are patentably distinct (MPEP § 806.04(h)). In the instant case, the intermediate product is deemed to be useful as intermediates for preparing e.g. carbacephems or oxacephems and the inventions are deemed patentably distinct since there is nothing on this record to show them to be obvious variants. Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions anticipated by the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

Art Unit: 1624

During a telephone conversation with John Thallemer on 5/27/05 a provisional election was made with traverse to prosecute the invention of Group I, claims 16-21, 23-27. Affirmation of this election must be made by applicant in replying to this Office action. Claim 22 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

*Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-21, 23-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. "Substituted" (e.g. R<sub>6p</sub> in claim 19) --- with what?

Art Unit: 1624

2. The term "acyl" is indefinite. Does this embrace acids of S? P? As? What does the stem look like, i.e. if the acyl is e.g. RC(O), what is R?
3. In choice 8 in claim 24, that should read "together are oxo", as the actual wording has each of them as oxo.
4. The claim 20 R'<sub>6p</sub> choice of H is not set forth in claim 1.
5. The claim 19 R<sub>6p</sub> and claim 6 R'<sub>6p</sub> and claim 20 R'<sub>6</sub> are broader than the claim 1 R<sub>6</sub>. Claim 1 does not permit the various choices such as alkyl to be substituted, but these claims do.
6. Also, the last choice depicted in claim 20, assuming that it really is a definition for the entire substituent, i.e. stands for R<sub>4</sub>, corresponds to Z in claim 1 as being NOH, but R<sub>7</sub> is not permitted to be OH. It is thus unclear what is actually intended.
7. Claim 17 is improperly dependent on claim 16. The R'<sub>6</sub> choices are broader in claim 2, e.g. substituted aryl or "heterocyclyl-carboximino".
8. Claim 19 has R<sub>2p</sub> and R<sub>3p</sub> as substituted alkyl, not seen in claim 16, making the claim improperly dependent on claim 1. It is thus unclear what is actually intended.
9. The way it is written, that last claim 20 structure is a choice for R'<sub>6p</sub>. That may not be what is intended.
10. The F atom in claim 18 is not provided for in claim 16, which has alkyl, not substituted alkyl. Likewise claim 20. It is thus unclear what is actually intended.
11. The R'<sub>6</sub> definition in claim 17 is garbled. Its hard to tell what is the choice for R'<sub>6</sub> and what is a substituent on the R'<sub>6</sub>.
12. Likewise claim 19 for R<sub>6p</sub>. The list uses both commas and semicolons. For example, what does the second "by" on line 16 refer to?

Art Unit: 1624

13. The terms "heterocyclyl-carboximino" near the end of claim 17 is unclear. What exactly is that?
14. In claim 16, line 1 of the  $R_6$  definition, a comma is missing after the hydrazino.
15. In heterocyclyl, what is the size of the ring? What is the number and nature of the heteroatoms? Can the ring be fused or spiroconnected to another ring, and if so, what kind of ring? Can the ring be bridged? Unsaturated?
16. The "interrupted" in claim 19 is unclear. Can this take place as the point of attachment? For example, could a  $C_1$  alkyl, interrupted by N, then be  $NH_2$ ?
17. In claim 19, line 16, the "ammonium" group present has no counterion, which is impossible.
18. In claim 5, line 17, "a carboxylic acid derivative" is unclear. Which carboxylic acid -- acetic acid? And what kind of derivative?
19. Likewise for "a sulfonic acid derivative" at line 17.
20. In claim 19, line 8 and elsewhere, condensed with what?
21. The alkenyl and alkynyl of claim 19 should be  $C_2$ , not  $C_1$ .
22. Interruption by N (claim 19, lines 13 and 15) is impossible. Since bonding in alkyl groups is always single, that would give a N with just two bonds.
23. The word "for" is probably missing after "defined" in last line of claim 19.
24. Claim 20, next to last line, should be "moiety", not "compound".
25. The "by" of ninth from last line of claim 19 is unclear. Should this be "substituted by"? Or "optionally substituted by"? Likewise next to last line of claim 19 and possibly elsewhere.

Art Unit: 1624

26. The moiety at the extreme upper left of IV in claim 25 is wrong. It should be  $\text{H}_2\text{N}^-$ , not  $\text{N}_2\text{H}^-$ .

27. The definition of Rint is garbled in claim 23. The formula shows that it is connected to the rest of the molecule via a double bond, but the structure given at the third from last line of claim shows just a single bond to the left.

28. Claim 23 is improperly dependent on claim 22. Claim 23 does not further limit claim 22 since these compounds do not fall within claim 22.

29. The definition of the extreme right hand side of the molecule in claim 23 is garbled. This is a moiety; what is in claim 22 is a series of molecules. It is impossible to tell what is actually intended for the right side of the moiety.

30. The intended meaning for "silyl" (e.g. choice 8 in claim 24) is unclear. Silyl is  $\text{SiH}_3$ , the group formed by the removal of a H from Silane,  $\text{SiH}_4$  and is a term analogous to methyl,  $\text{CH}_3$ . It does not appear likely that such a group is intended.

31. Claim 26 sets forth the salt, but claim 16 makes no provision for a salt in the first place.

32. Claim 27 has the wrong term. This covers bacteria, viruses, fungi, protozoa, etc, which is not what these compounds will be effective against. Suggested is bacterial.

Claims 16-17, 24, 26 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Art Unit: 1624

A. The removal of the two original provisos expands the claims beyond what the specification provides for. The claims as amended now permit  $R_4 = H$ ,  $R_1 = H$  or methyl. The claims also permit  $R_2=R_3=R_4$ . Neither of these three subgenuses were originally permitted; now these are permitted some of the time, since the new provisos only partially exclude such compounds.

B. The 6 new provisos lack description. Even a negative limitation requires description, *Ex Parte Grasselli*, 231 USPQ 393. These introduce new concepts, such as provisos depending on the value of V and W, and provisos depending whether or not  $R_1$  is  $CH_2F$ .

*Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 20 is rejected under 35 U.S.C. 102(b) as being anticipated by WO 96/35692.

Claim 20  $R'_{6p}$  choice of H means that species 115 on page 45, which has  $R_{1p} = R_5 = H$ ,  $W = CH$  anticipates the claim.

*Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a

Art Unit: 1624

person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 16-19, 21, 23-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/35692.

The current claims fall within the genus of the reference, and hence they are obvious. Several species of the reference are extremely close in structure. Specifically:

A. Species 115 corresponds to R<sub>4</sub> as formyl (i.e. R<sub>6</sub> as H), whereas claim 1 has R<sub>4</sub> as acetyl (i.e. R<sub>6</sub> as CH<sub>3</sub>). Likewise species 50 and 67, which are the same except that these have R<sub>3</sub> or R<sub>2</sub> as methyl. Applicants are thus claiming a homolog. Compounds that differ only by the presence or absence of an extra methyl group or two are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologue. As was stated in *In re Grose*, 201 USPQ 57, 63, "The known structural relationship between adjacent homologues, for example, supplies a chemical theory upon which a *prima facie* case of obviousness of a compound may rest." The homologue is expected to be preparable by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious even in the absence of a specific teaching to add or remove methyl groups. See *In re Wood*, 199 USPQ 137; *In re Hoke*, 195 USPQ 148; *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re Wiechert*, 152 USPQ 249; *Ex parte Henkel*, 130 USPQ 474; *In re Jones*, 74 USPQ 152, 154; *Ex Parte Fischer* 96 USPQ 345; *In re Fauque*, 121 USPQ 425; *In re Druey*, 138 USPQ 39; *Ex parte Fischer*, 96 USPQ 345; *in re Bowers and Orr*, 149 USPQ 570. In all of these cases,

Art Unit: 1624

the close structural similarity between two compounds differing by one or two methyl groups was itself sufficient show obviousness. Note also *In re Jones*, 21 USPQ2d 1942, which states at 1943 "Particular types or categories of structural similarity without more, have, in past cases, given rise to *prima facie* obviousness"; one of those listed is "adjacent homologues and structural isomers". Similar is *In re Schechter and LaForge*, 98 USPQ 144, 150, which states "a novel useful chemical compound which is homologous or isomeric with compounds of the prior art is unpatentable unless it possesses some unobvious or unexpected beneficial property not possessed by the prior art compounds." Note also *In re Deuel* 34 USPQ2d 1210, 1214 which states, "Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologs because homologs often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties." See also MPEP 2144.09, second paragraph.

B. Species 42, 66 are eliminated by the proviso in the last line of claim 1. However:

- a) These species are homolog of the corresponding ethyl compounds (i.e. where R<sub>1</sub> in the claims is ethyl) which are not eliminated by the proviso.
- b) The reference teaches, and example 139 exemplifies, the choice of CH<sub>2</sub>F rather than CH<sub>3</sub>. Thus, such a variation would be obvious.

C. Species 139 is eliminated by the proviso of the next to last line of claim 1. However, a methylated version of this, with the methyl on either of the guanidine N atoms, would avoid the proviso. Such a variation is considered obvious because of the close structural similarity. See *In re Hoeksema*, 154 USPQ 169; *Ex parte Weston*, 121 USPQ 428; *Ex parte*

Art Unit: 1624

*Bluestone*, 135 USPQ 199; *In re Doebl*, 174 USPQ 158. Further, the reference has examples of such methylation in species 42, 50, 67. Hence, such a modification is clearly taught by the reference.

The synthesis is the same.

### *Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 16-21, 23-27 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and others of U.S. Patent No. US 6531465 B1. Although the conflicting claims are not identical, they are not patentably distinct from each other because there is no patentable line of distinction. The claims overlap. Note especially species 122 of the patent, which falls within the rejected claims as well as claim 1 of the patent, and species 115, which falls in claim 1 of the patent and in claim 20 here. Note also species 2 and 3 of claim 5 of the patent. These two species are excluded by choices d) and f). However, the rejected claims cover homologs of such species, e.g. species with R4 as methyl rather than H, which is obvious as a homolog

Art Unit: 1624

for reasons set forth above. Further, the reference itself teaches such equivalence, note comparison of the aforementioned species 122 and 139.

Claims 16-21, 23-27 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 and others of copending Application No. 10308331. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the same issues. The claims are pretty much the same as in the patent, since the patent is the parent to 10308331.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 16-21, 23-24, 26-27 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of U.S. Patent No. 6693095. Although the conflicting claims are not identical, they are not patentably distinct from each other because the parent patent heavily overlaps with the instant claims. Note for example that patent claim 2 is a species (and esters thereof) which is not excluded by any proviso.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 571-272-0663. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on (571)272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1624

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read "Mark L. Berch". The signature is fluid and cursive, with the first name "Mark" and last name "Berch" clearly distinguishable.

Mark L. Berch  
Primary Examiner  
Art Unit 1624

5/31/05